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EXAMINER	
WHITE,E	
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DATE MAILED: 11/03/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☒ Responsive to communication filed on 6/26/1995 ☒ This action is made final.

A shortened statutory period for response to this action is set to expire three month(s), ~~_____~~ days from the date of this letter.
Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☐ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474..
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1-17 and 19 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☐ Claims _____ have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1-17 and 19 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

Claims 1-17 are pending in the instant application.

Claims 1, 2, 9 and 12-14 are rejected under 35 U.S.C. § 112, first paragraph, as the disclosure is enabling only for claims limited hyaluronic acid having a molecular weight range of 550,000 to 8,000,000 (see page 6, lines 26-30 of the specification). There appears to be no reference to other polysaccharides having this molecular weight range. Hence, the above cited claims are enabling only for a portion of the subject matter claimed. See M.P.E.P. §§ 706.03(n) and 706.03(z).

Applicant's arguments with respect to claims 1, 2, 9 and 12-14 have been considered but are deemed to be moot in view of the new grounds of rejection.

The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. § 103, the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 C.F.R. § 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of potential 35

U.S.C. § 102(f) or (g) prior art under 35 U.S.C. § 103.

Claims 1-6, 8, 13-16 and 19 are rejected under 35 U.S.C. § 103 as being unpatentable over Galatik et al (Czechoslovak Patent No. 264,719, see translated copy).

The Galatik et al Patent discloses a pharmacological preparation which contains a complex of a hyaluronate of an alkali metal with a multivalent cation selected from the group Mg^{2+}, Ca^{2+}, Zn^{2+}, Ba^{2+}, Al^{3+}, Cu^{2+}, Zr^{4+}, Cr^{3+}, Fe^{3+}, alone or in a mixture with physiological salt solution, where the molar composition of the complex is 0.1 to 5 moles of the hyaluronate to 1 to 25 moles of the coordinated cation (see page 2, last paragraph of the translated copy). The Galatik et al Patent discloses the preparation as being used to prevent postoperative adhesion of tendons and conjunctival sacs (see page 2, 2nd paragraph of the translated copy). It would have been obvious to one of ordinary skill in the art having the Galatik et al Reference before him to use an effective amount of a carboxyl-containing polysaccharide or a pharmacologically acceptable salt thereof in a method of reducing the incidence of post-operative adhesion formation in an animal as instantly claimed in view of their closely related structures and the resulting expectation of similar anti-adhesive properties.

Applicant's arguments filed June 26, 1995 have been fully considered but they are not deemed to be persuasive. Applicants further limit the claims by disclosing a molecular weight range of 550,000 to about 8,000,000 and sets forth a limitation in the

claims to indicate that a trivalent cation is provided in an amount sufficient to crosslink in the range of from about 60 to 100 percent of the carboxyl groups of the carboxyl containing polysaccharide. However, the limitations do not over come the above rejection since molar proportions or ranges of molecular weight cannot be the basis for patentability of subject matter encompassed by the prior art where there is nothing to indicate such proportion or range is critical.

Also noted is the Declaration of Douglas B. Johns under 37 C.F.R. §1.132 filed June 26, 1995. The Declaration points out that the Galatik et al Reference describes complexes of hyaluronate of an alkali metal with multivalent cations whereby the molar composition of the complex is 0.1 to 5 moles of hyaluronate to 1 to 25 moles of coordinate cations and indicates that this is equivalent to a range of 0.2 moles to 250 moles of cation per mole of hyaluronate. In the Declaration the examples presented in the Galatik et al Reference were examined to determine whether a monomer or polymer formed the basis of the calculations. Applicants conclude from the calculation presented in the Declaration that the maximum amount of cations used by Galatik et al would be sufficient to theoretically crosslink less than 60 percent of the carboxyl groups of a hyaluronate polymer with an average molecular weight of 550,000 or greater. Applicants additionally argue that the Galatik et al Reference is nonenabling for hyaluronate with a molecular weight range of 550,000 to 8,000,000 daltons. However, this argument and the

declaration are not persuasive since the Galatik et al Reference discloses a complex of a hyaluronate of an alkali metal with a multivalent cation which is capable of crosslinking 60 to 100 percent of the carboxyl groups of the carboxyl-containing polysaccharide which may have a molecular weight (MW) outside the claimed MW range. It is noted on page 6, lines 26-28 of the specification that the average molecular weight of HA is preferably in the range of from about 550,000 to 8,000,000. If criticality is asserted for proportions or ranges, the specification must not disclose them as merely preferred. See Hays v. Reynolds, Comr. Pats. (DCDC 1965) 242 FSupp 206, 145 USPQ 665; In re Bourdon (CCPA 1957) 240 F2d 358, 112 USPQ 323. Unless the allegations of the criticality of the limitations recited in the rejected claims are supported by actual proof, they cannot be given any weight in determination of the issue of obviousness.

Claims 7 and 17 are rejected under 35 U.S.C. § 103 as being unpatentable over Galatik et al (Czechoslovak Patent No. 264,719, see translated copy) as applied to Claims 1-6, 8 and 13-16 above, and further in view of Balazs (US Patent No. 4,141,973) and Shimizu et al (US Patent No. 4,024,073).

As disclosed above, the Galatik et al Patent discloses a hyaluronate complex of an alkali metal with a multivalent cation selected from the group Mg^{2+}, Ca^{2+}, Zn^{2+}, Ba^{2+}, Al^{3+}, Cu^{2+}, Zr^{4+}, Cr^{3+}, Fe^{3+}, which can be used to prevent postoperative adhesion of tendons and conjunctival sacs. However, the Galatik et al Patent

does not disclose information with regard to viscosity and administration of the hyaluronate complex.

The Balazs Patent discloses molecular weights of hyaluronic acid which are within the scope of the molecular weights of the hyaluronic acid disclosed in the specification and also suggests viscosity values of hyaluronic acid which are within the scope of the adhesion preventative disclosed in the instant claims. (see column 4, lines 44-57 of the Balazs Patent).

Shimizu et al disclose a hydrogel which comprises a water-soluble polymer containing a chelating agent bound to a polymer chain and a metal ion having a valance of 2 or above, whereby the polymers are cross-linked through chelation between two chelating agents by the polyvalent metal ion. Shimizu et al further disclose that the polymer may be selected as hyaluronic acid (see column 1, lines 55 and 56). Shimizu et al disclose that the hydrogel-drug can be used in various ways which include injection and surgical use, which is within the scope of instant claim 7 whereby the adhesion preventative is applied directly to the site of surgical trauma in one application.

It would have been obvious to one having ordinary skill in the art at the time the invention was made to used the hyaluronate complex to prevent postoperative adhesion of tendons and conjunctival sacs as disclosed by Galatik et al and to apply the hyaluronate complex by injection with a syringe as suggested by Shimizu et al and to used an adhesion preventative having a viscosity of 2,500 cps to about 250,000 cps since Balazs shows

that hyaluronic acid having such viscosity values is well known in the art.

Applicant's arguments filed June 26, 1995 have been fully considered but they are not deemed to be persuasive. The Balazs Patent is cited to show that the instant claimed molecular weight and viscosity values of hyaluronic acid are well known in the art. The Shimizu et al Patent is cited to show that surgical use of complexes of hyaluronic acid is well known in the art.

Claims 9-12 are rejected under 35 U.S.C. § 103 as being unpatentable over Galatik et al (Czechoslovak patent No. 264,719, see translated copy) as applied to claims 1-6 and 8 above, and further in view of Applicants's own disclosure at page 10, lines 15-27 of the specification.

Galatik et al is as discussed above. The specification at page 10 discloses that it is well known that tolmetin and other NSAIDS are adhesion preventatives. Therefore, it would have been prima facie obvious to one of ordinary skill in the art to combine two compositions each one of which is taught by prior art to be useful for the same purpose in order to form a third composition to be used for the same purpose, In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).

Applicant's arguments filed June 26, 1995 have been fully considered but they are not deemed to be persuasive. See the argument above regarding the Galatik et al Reference.

All the claims (1-17 and 19) are rejected.

Applicant's amendment necessitated the new grounds of rejection. Accordingly, **THIS ACTION IS MADE FINAL.** See M.P.E.P. § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 C.F.R. § 1.136(a).

A SHORTENED STATUTORY PERIOD FOR RESPONSE TO THIS FINAL ACTION IS SET TO EXPIRE THREE MONTHS FROM THE DATE OF THIS ACTION. IN THE EVENT A FIRST RESPONSE IS FILED WITHIN TWO MONTHS OF THE MAILING DATE OF THIS FINAL ACTION AND THE ADVISORY ACTION IS NOT MAILED UNTIL AFTER THE END OF THE THREE-MONTH SHORTENED STATUTORY PERIOD, THEN THE SHORTENED STATUTORY PERIOD WILL EXPIRE ON THE DATE THE ADVISORY ACTION IS MAILED, AND ANY EXTENSION FEE PURSUANT TO 37 C.F.R. § 1.136(a) WILL BE CALCULATED FROM THE MAILING DATE OF THE ADVISORY ACTION. IN NO EVENT WILL THE STATUTORY PERIOD FOR RESPONSE EXPIRE LATER THAN SIX MONTHS FROM THE DATE OF THIS FINAL ACTION.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to E. White whose telephone number is (703) 308-4621.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

E. White
White
October 24, 1995

DOUGLAS W. ROBINSON
SUPERVISORY PATENT EXAMINER
GROUP 1800